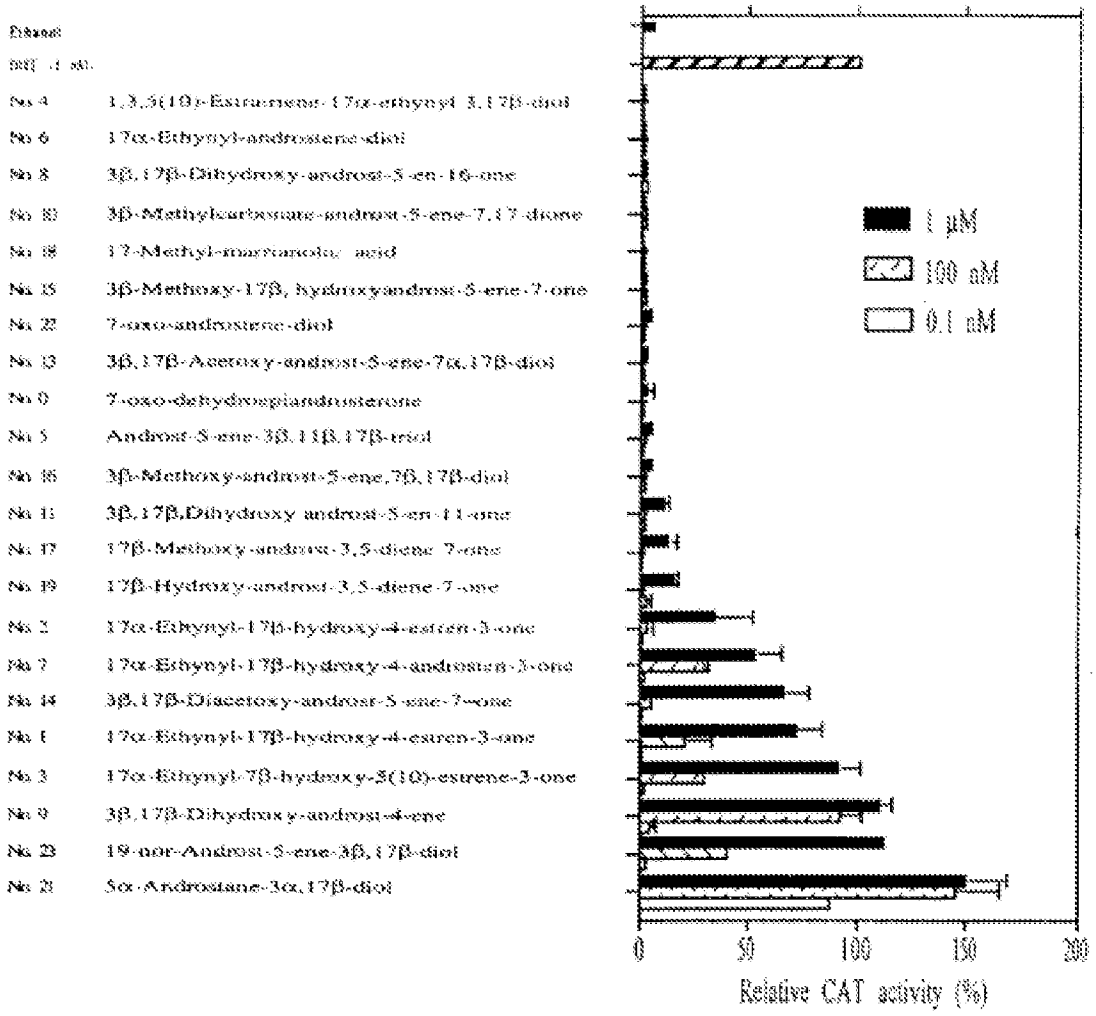
AMENDMENTS TO THE SPECIFICATION

The following paragraphs replace paragraphs to be deleted which are on pages 79 through 80 and are identified from the following words from the beginning and end of each paragraph. Example 2. ….. CAT gene transcription.; Example 3. …. they have no effect.; Example 4. …. at 1 μM (figure 3).; Example 5. …. activity by about 75%.

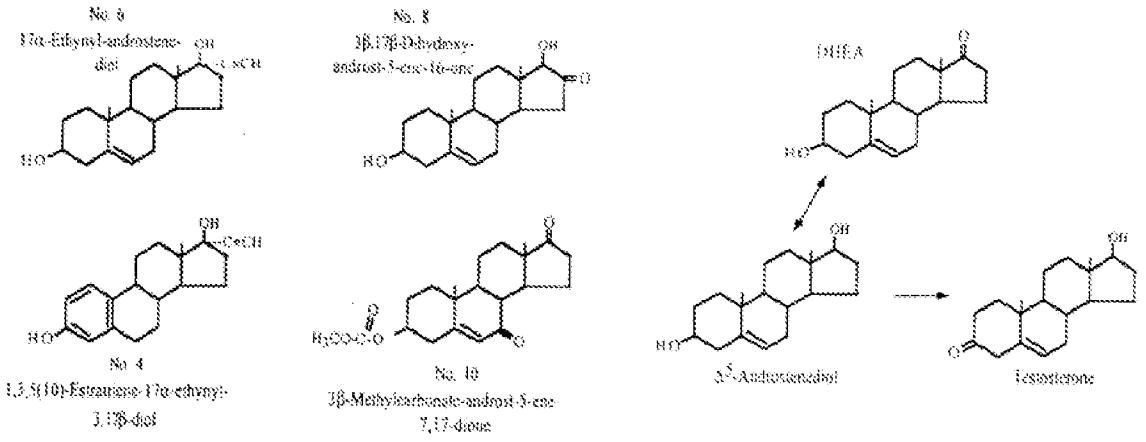
Example 2. Induction of AR-mediated transcriptional activity.

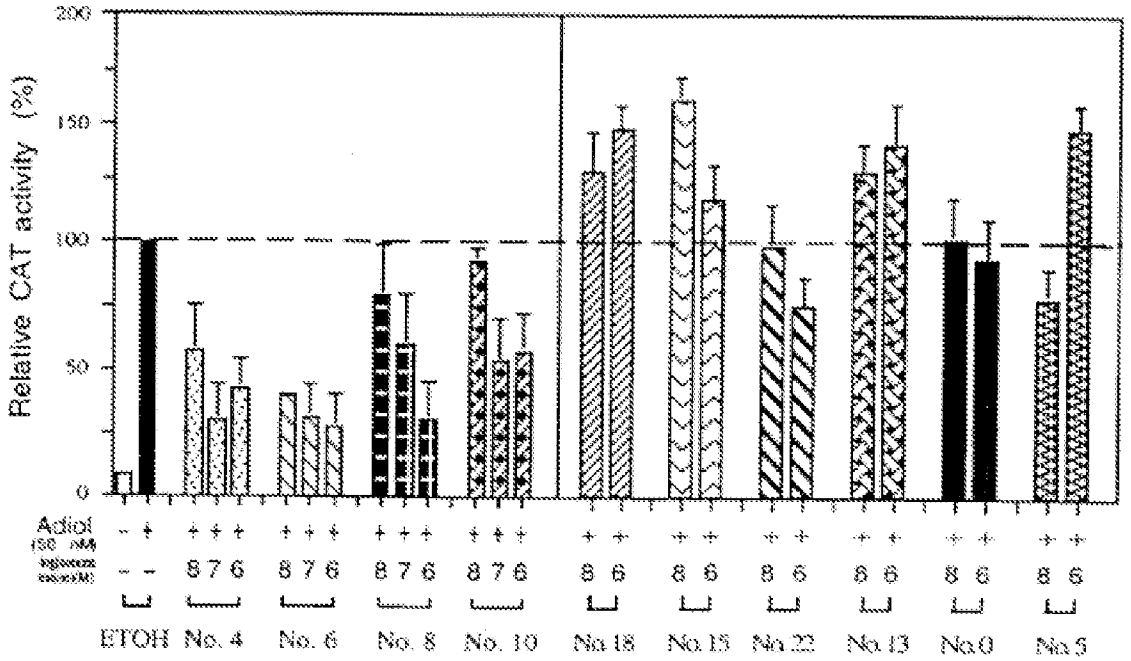


Steroid compounds were screened for their ability to induce AR transcriptional activity in the AR-negative PC-3 cell line. The results of the CAT assay were obtained by transient co-transfection of AR plasmid and a reporter plasmid

(MMTVCAT) containing the CAT gene linked to the androgen response element (ARE). After transfection, the cells were treated with various DHEA derivatives at 1000, 10, and 0. 1 nM. As shown ~~in figure 1~~ above, compounds 0, 4, 5, 6, 8, 10, 13, 15, 16, 18, and 22 had little androgenic activity but they did induce a low level of AR-mediated CAT gene transactivation. AED (compound 21) had about the same capacity as DHT to stimulate AR-mediated CAT gene transcription.

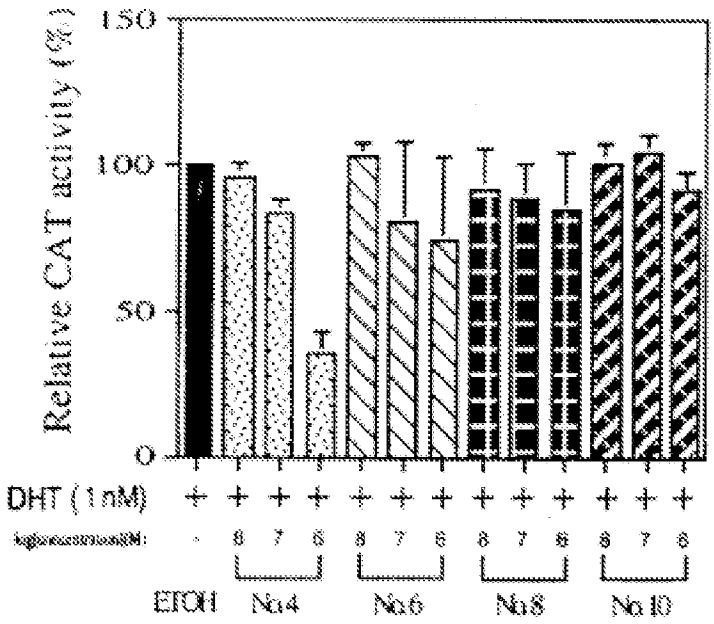
Example 3. Identification of anti-adiol activity of steroids with low androgenic effects.





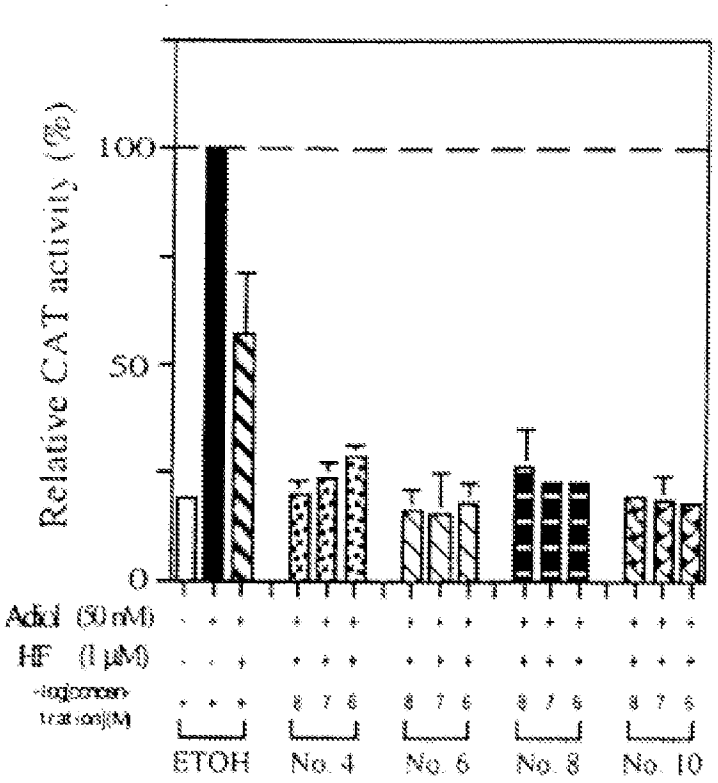
Several compounds were screened for their capacity to modulate AED's effects on AR-mediated activation of gene transcription in PC-3 cells. The chemical structures of compounds 4, 6, 8 and 10 are shown ~~in figure 2A~~ above. The PC-3 cells were co-transfected with pSG5 and the MMTV-CAT reporter vector in the presence of 50 nM AED and each compound at a concentration of 10, 100, or 1000 nM. As shown ~~in figure 2B~~ above, compounds 4, 6, 8 and 10 antagonized AED-mediated AR transcriptional activity. At concentrations of 0.1 μM and 1 μM, compounds 4 and 6 suppressed the AED-induced AR transactivation to less than 30%. Compounds 0, 5, 13, 15, 18 and 22 show either activation of AED-mediated AR transcriptional activity or they have no effect.

Example 4. Identification of anti-DHT effects of steroids.



Compounds 4, 6, 8 and 10 were examined to determine whether these AED antagonists had the ability to repress DHT-induced AR transactivation. PC-3 cells were co-transfected with pSG5 and the MMTV-CAT reporter plasmid in the presence of 1 nM DHT and each compound at 10, 100, or 1000 nM. Compound 4 repressed the DHT-induced AR transactivation to less than 40% at 1 μM ~~(figure 3)~~ as shown above.

Example 5. Suppression of the AED-induced AR transcriptional activity in the presence of HF.



To mimic the *in vivo* condition of total androgen blockage in prostate cancer patients, compounds 4, 6, 8 and 10 were examined for their capacity to antagonize AED-induced AR transactivation in the presence of HF. In the presence of 1 μM HF, 50 nM AED, and each compound at 0.01, 0.1 or 1 μM, PC-3 cells were transiently transfected with pSG5 and the MMTV-CAT reporter plasmid. As shown ~~in figure 4~~ above, HF suppressed AED-mediated AR transcription activity by about 40%. The compounds tested decreased AED-mediated AR transcription activity by about 75%.